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=> s cholesteryl ester transfer protein
L1         5417 CHOLESTERYL ESTER TRANSFER PROTEIN

=> s l1 and administration
L2          268 L1 AND ADMINISTRATION

=> s l2 and human
L3          192 L2 AND HUMAN

=> dup remove l3
PROCESSING COMPLETED FOR L3
L4          125 DUP REMOVE L3 (67 DUPLICATES REMOVED)

=> s l4 and HDL
L5           93 L4 AND HDL

=> s l5 and LDL
L6           60 L5 AND LDL

=> s l6 and "CETP"
L7           44 L6 AND "CETP"

=> dup remove l7
PROCESSING COMPLETED FOR L7
L8           44 DUP REMOVE L7 (0 DUPLICATES REMOVED)

=> d l8 1-44 cbib abs

L8   ANSWER 1 OF 44  CAPLUS  COPYRIGHT 2005 ACS on STN
2005:324140  Preparation of quinoline glucuronides as cholesteryl
     ester transfer protein (CETP)
     inhibitors and metabolites.  Dalvie, Deepak Kamalnath; Ruggeri, Roger
     Benjamin (Pfizer Products Inc., USA).  PCT Int. Appl. WO 2005033082 A2
     20050414, 45 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA,
     BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,
     EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
     KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
     NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
     TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT,
     BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE,
     IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.  (English).  CODEN:
     PIXXD2.  APPLICATION: WO 2004-IB3054 20040920.  PRIORITY: US 2003-PV507385
     20030930.
GI
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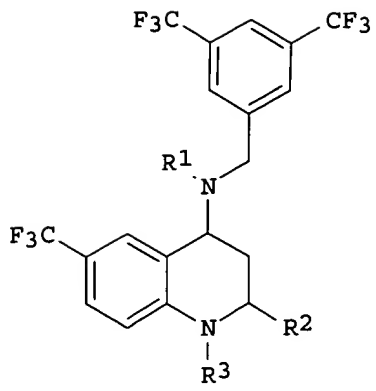

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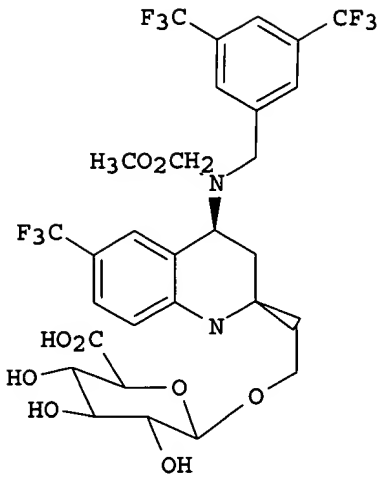

II

AB Compds. I were prepared, wherein R1 is -CO2CH3 or -H; R2 is -CH2CH3, -CH2CH2OH, -CH2CO2H, -CH2CO2A, and - CH2CH2OA; wherein A is 3,4,5-trihydroxytetrahydropyran-2-carboxylic acid; and R3 is -H, -CO2CH2CH3, -CO2CH2CH2OH, -CO2CH2CO2H, - CO2CH2CH2OA and -CO2CH2CO2A; or a pharmaceutically acceptable salt of said compound with the proviso that if R1 is -CO2CH and R3 is -H, then R2 is not -CH2CH3, -CH2CH2OH, or -CH2CO2H; if R1 is -CO2CH3 and R3 is -CO2CH2CH3, then R2 is not -CH2CH3, -CH2CH2OH, or -CH2CO2H; and if R1 is -CO2CH3 and R2 is -CH2CH3, then R3 is not -CO2CH2CH2OH, or -CO2CH2CO2H, resulting from the **administration** of torcetrapib to a mammal, and the use of such compds. as an indicator or bio-marker to the presence or exposure of torcetrapib in the plasma of a mammal including **humans.** The invention is also directed to **cholesteryl ester transfer protein** (**CETP**) inhibitors, pharmaceutical compns. containing such inhibitors and the use of such inhibitors to elevate cert in plasma lipid levels, including high d. lipoprotein (**HDL**)-cholesterol and t lower certain other plasma lipid levels, such as low d. lipoprotein (**LDL**)-cholesterol and triglycerides. Thus, uronic acid II was prepared as **cholesteryl ester transfer protein** inhibitor. Title compds. are useful for the treatment and correction of the various dyslipidemias observed to be associated with the development and incidence of atherosclerosis and cardiovascular disease, including hypo-α-lipoproteinemia, hyper-β-lipoproteinemia, hypertriglyceridemia, and hypercholesterolemia.

L8 ANSWER 2 OF 44 MEDLINE on STN

2004611388. PubMed ID: 15585212. Effects of increasing doses of simvastatin on fasting lipoprotein subfractions, and the effect of high-dose simvastatin on postprandial chylomicron remnant clearance in normotriglyceridemic patients with premature coronary sclerosis. van Wijk J P H; Buirma R; van Tol A; Halkes C J M; De Jaegere P P Th; Plokker H W M; van der Helm Y J M; Castro Cabezas M. (Department of Vascular Medicine, University Medical Center Utrecht, The Netherlands.) Atherosclerosis, (2005 Jan) 178 (1) 147-55. Journal code: 0242543. ISSN: 0021-9150. Pub. country: Ireland. Language: English.

AB Postprandial hyperlipidemia has been linked to premature coronary artery disease (CAD) in fasting normotriglyceridemic patients. We investigated the effects of increasing doses of simvastatin up to 80 mg/day on fasting and postprandial lipoprotein metabolism in 18 normotriglyceridemic patients with premature CAD. Fasting lipoprotein subfractions and **cholesteryl ester transfer protein** (

CETP) activity were determined after each 5-week dose titration (0, 20, 40 and 80 mg/day). At baseline and after treatment with simvastatin 80 mg/day, standardised Vitamin A oral fat loading tests (50 g/m2; 10 h) were carried out. Ten normolipidemic healthy control subjects matched for gender, age and BMI underwent tests without medication. Treatment with simvastatin resulted in dose-dependent reductions of fasting **LDL**-cholesterol, without changing cholesterol levels in the VLDL-1, VLDL-2 and IDL fractions. In addition, simvastatin decreased **CETP** activity dose-dependently, although **HDL**-cholesterol remained unchanged. Simvastatin 80 mg/day decreased fasting plasma triglycerides (TG) by 26% ($P < 0.05$), but did not decrease significantly TG levels in any of the subfractions. The TG/cholesterol ratio increased in all subfractions. The plasma TG response to the oral fat loading test, estimated as area under the curve (TG-AUC), improved by 30% (from 21.5 +/- 2.5 to 15.1 +/- 1.9 mmol h/L; $P < 0.01$). Treatment with simvastatin 80 mg/day improved chylomicron remnant clearance (RE-AUC) by 36% from 30.0 +/- 2.6 to 19.2 +/- 3.3 mg h/L ($P < 0.01$). After therapy, remnant clearance in patients was similar to controls (19.2 +/- 3.3 and 20.3 +/- 2.7 mg h/L, respectively), suggesting a normalization of this potentially atherogenic process. In conclusion, high-dose simvastatin has beneficial effects in normotriglyceridemic patients with premature CAD, due to improved chylomicron remnant clearance, besides effective lowering of **LDL**-cholesterol. In addition, the lipoprotein subfractions became more cholesterol-poor, as reflected by the increased TG/cholesterol ratio, which potentially makes them less atherogenic.

L8 ANSWER 3 OF 44 EMBASE
on STN

2005122818 EMBASE Inhibitors of **cholesteryl ester transfer protein** - A step forward in the treatment of coronary artery disease?. Doggrell S.A.. S.A. Doggrell, School of Biomedical Sciences, University of Queensland, Brisbane, QLD 4072, Australia. s_doggrell@yahoo.com. Drugs of the Future Vol. 30, No. 1, pp. 45-50 2005.
Refs: 28.
ISSN: 0377-8282. CODEN: DRFUD4
Pub. Country: Spain. Language: English. Summary Language: English.

ED Entered STN: 20050407

AB Although the **LDL** cholesterol-lowering statins have reduced the mortality and morbidity associated with coronary artery disease (CAD), considerable mortality and morbidity remains. Increasing **HDL** cholesterol levels is associated with reduced CAD mortality and morbidity. In healthy subjects with mild dyslipidemia, treatment with JTT-705 decreased **cholesteryl ester transfer protein** (**CETP**) activity, increased **HDL** cholesterol and decreased **LDL** cholesterol. Similarly, another **CETP** inhibitor, torcetrapib, has recently been shown to increase **HDL** cholesterol by 46%, decrease **LDL** cholesterol by 8% and have no effect on triglycerides in subjects with **HDL** cholesterol levels below 1.0 mmol/l. Increasing **HDL** cholesterol with inhibitors of **CETP** represents a new approach to dyslipidemia that requires further investigation, especially in patients with CAD.

L8 ANSWER 4 OF 44 EMBASE
on STN

2004437464 EMBASE Regulation of plasma high-density lipoprotein levels by the ABCA1 transporter and the emerging role of high-density lipoprotein in the treatment of cardiovascular disease. Brewer Jr. H.B.; Remaley A.T.; Neufeld E.B.; Basso F.; Joyce C.. H.B. Brewer Jr., Molecular Disease Branch, NHLBI, National Institutes of Health, 10 Center Drive, Bethesda, MD 20892, United States. bryan@mdb.nhlbi.nih.gov. Arteriosclerosis, Thrombosis, and Vascular Biology Vol. 24, No. 10, pp. 1755-1760 2004.
Refs: 73.
ISSN: 1079-5642. CODEN: ATVBFA

Pub. Country: United States. Language: English. Summary Language: English.
ED Entered STN: 20041112
AB High-density lipoproteins (**HDL**) protect against cardiovascular disease. **HDL** removes and transports excess cholesterol from peripheral cells to the liver for removal from the body. **HDL** also protects low-density lipoproteins (**LDL**) from oxidation and inhibits expression of adhesion molecules in endothelial cells, preventing monocyte movement into the vessel wall. The ABCA1 transporter regulates intracellular cholesterol levels in the liver and in peripheral cells by effluxing excess cholesterol to lipid-poor apoA-I to form nascent **HDL**, which is converted to mature alpha;-**HDL** by esterification of cholesterol to cholesteryl esters (CE) by lecithin cholesterol acyltransferase. The hepatic ABCA1 transporter and apoA-I are major determinants of levels of plasma α- **HDL** cholesterol as well as poorly lipidated apoA-I, which interact with ABCA1 transporters on peripheral cells in the process of reverse cholesterol transport. Cholesterol in **HDL** is transported directly back to the liver by **HDL** or after transfer of CE by the **cholesteryl ester transfer protein** (**CETP**) by the apoB lipoproteins. Current approaches to increasing **HDL** to determine the efficacy of **HDL** in reducing atherosclerosis involve acute **HDL** therapy with infusions of apoA-I or apoA-I mimetic peptides and chronic long-term therapy with selective agents to increase **HDL**, including **CETP** inhibitors.

L8 ANSWER 5 OF 44 MEDLINE on STN
2004168305. PubMed ID: 15064100. The relationship between **cholesteryl ester transfer protein** levels and risk factor profile in patients with familial hypercholesterolemia. de Grooth Greetje J; Smilde Tineke J; Van Wissen Sanne; Klerkx Anke H E M; Zwinderman Aeilko H; Fruchart Jean-Charles; Kastelein John J P; Stalenhoef Anton F H; Kuivenhoven Jan Albert. (Department of Vascular Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands.) Atherosclerosis, (2004 Apr) 173 (2) 261-7. Journal code: 0242543. ISSN: 0021-9150. Pub. country: Ireland. Language: English.
AB BACKGROUND: **Cholesteryl ester transfer protein** (**CETP**) mediates the transfer of neutral lipids between lipoproteins. The role of **CETP** in atherogenesis is controversial. To better understand the relationships between plasma **CETP** levels, lipoproteins and atherosclerosis, we assessed these parameters in patients with an enhanced risk for atherosclerosis. METHODS AND RESULTS: We investigated 281 patients with familial hypercholesterolemia (FH) in which the effects of two statins were compared in a 2-year, randomized, double-blinded study. Patients were stratified in quartiles according to their **CETP** baseline levels. In addition to correlations with decreased high-density lipoprotein cholesterol (**HDL**-c), increased low-density lipoprotein cholesterol (**LDL**-c) and enhanced triglyceride levels, higher **CETP** levels were also associated with reduced **HDL** particle size, and smaller and denser **LDL**. Statins reduced plasma **CETP** levels and atherogenic lipoproteins. Nevertheless, baseline **CETP** concentration was positively associated with IMT after 2 years of therapy. CONCLUSION: This study provides evidence that **CETP** levels are associated with a more atherogenic lipid profile and increased progression of atherosclerosis. Statin treatment improved the lipoprotein profile in FH patients, but to a lesser extent in those with high **CETP** levels. These findings might imply that statin treatment does not entirely counteract the lipoprotein abnormalities associated with high **CETP** levels.

L8 ANSWER 6 OF 44 EMBASE on STN
2004061232 EMBASE An ω-3 Polyunsaturated Fatty Acid Concentrate Increases Plasma High-Density Lipoprotein 2 Cholesterol and Paraoxonase

Levels in Patients with Familial Combined Hyperlipidemia. Calabresi L.; Villa B.; Canavesi M.; Sirtori C.R.; James R.W.; Bernini F.; Franceschini G.. Prof. G. Franceschini, Center E. Grossi Paoletti, Dept. of Pharmacological Sciences, Via Balzaretti 9, 20133 Milano, Italy. Metabolism: Clinical and Experimental Vol. 53, No. 2, pp. 153-158 2004. Refs: 51.
ISSN: 0026-0495. CODEN: METAAJ
Pub. Country: United States. Language: English. Summary Language: English.
ED Entered STN: 20040304
AB A remarkable reduction of plasma concentrations of high-density lipoproteins (**HDL**), especially of the **HDL**(2) subfraction, is one of the typical lipoprotein alterations found in patients with familial combined hyperlipidemia (FCHL). Fourteen FCHL patients received 4 capsules daily of Omacor (an ω-3 polyunsaturated fatty acid [ω3 FA] concentrate providing 1.88 g of eicosapentaenoic acid [EPA] and 1.48 g of docosahexaenoic acid [DHA] per day; Pronova Biocare, Oslo, Norway) or placebo for 8 weeks in a randomized, double-blind, crossover study. Plasma triglycerides were 44% lower, and **LDL** cholesterol and apoliporpotein (apo)B were 25% and 7% higher after Omacor than placebo. **HDL** cholesterol was higher (+8%) after Omacor than placebo, but this difference did not achieve statistical significance. Omacor caused a selective increase of the more buoyant **HDL**(2) subfraction; plasma **HDL**(2) cholesterol and total mass increased by 40% and 26%, respectively, whereas **HDL**(3) cholesterol and total mass decreased by 4% and 6%. Both **HDL**(2) and **HDL**(3) were enriched in cholesteryl esters and depleted of triglycerides after Omacor. No changes were observed in the plasma concentration of major **HDL** apolipoproteins, LpA-I and LpA-I:A-II particles, lecithin:cholesterol acyltransferase (LCAT), and **cholesteryl ester transfer protein** (**CETP**). The plasma concentration of the **HDL**-bound antioxidant enzyme paraoxonase increased by 10% after Omacor. Omacor may be helpful in correcting multiple lipoprotein abnormalities and reducing cardiovascular risk in FCHL patients.

L8 ANSWER 7 OF 44 MEDLINE on STN
2003188500. PubMed ID: 12706483. **Cholesteryl ester transfer protein** activity and atherogenic parameters in rabbits supplemented with cholesterol and garlic powder. Kwon Myung-Ja; Song Young-Sun; Choi Myung-Sook; Park Sang-Joon; Jeong Kyu-Shik; Song Yeong-Ok. (Department of Food Science and Nutrition, Pusan National University, 609-735, Busan, South Korea.) Life sciences, (2003 May 16) 72 (26) 2953-64. Journal code: 0375521. ISSN: 0024-3205. Pub. country: England: United Kingdom. Language: English.
AB The current study was conducted to examine the effect of garlic supplementation on **CETP** activity, along with its anti-atherosclerotic effect in cholesterol-fed rabbits. Rabbits were fed a 1% cholesterol diet for 12 weeks, including a 1% garlic powder supplement. The garlic-supplemented group exhibited significantly lower **CETP** activity than the control group during the experimental period ($P < 0.05$). Among the atherogenic parameters, the total cholesterol, TG, **LDL**-C, VLDL-C, and atherogenic index were all significantly lower in the garlic group than in the control group during the experimental period ($P < 0.05$), whereas the **HDL**-C concentration was significantly higher in the garlic group than in the control group after 12 weeks ($P < 0.05$). Atherosclerotic lesion area in the aorta arch was also significantly lower in the garlic group ($P < 0.05$). In the morphological examination, the garlic-supplemented group exhibited far fewer fat droplet deposits than the control group. Furthermore, the garlic supplement also lowered the aortic and hepatic cholesterol, and triglyceride. Accordingly, the current results suggest that garlic exerts hypocholesterolemic and/or antiatherogenic and that plasma **CETP** activity might be a risk marker related with atherogenesis. As such, the inhibition of **CETP** activity may

delay the progression of atherosclerosis, thereby supporting the atherogenicity of **CETP** and the inhibitory activity of garlic supplementation against **CETP**.

L8 ANSWER 8 OF 44 MEDLINE on STN
2003226761. PubMed ID: 12747787. Discovery of a simple picomolar inhibitor of **cholesteryl ester transfer protein**. Reinhard Emily J; Wang Jane L; Durley Richard C; Fobian Yvette M; Grapperhaus Margaret L; Hickory Brian S; Massa Mark A; Norton Monica B; Promo Michele A; Tollefson Michael B; Vernier William F; Connolly Daniel T; Witherbee Bryan J; Melton Michele A; Regina Karen J; Smith Mark E; Sikorski James A. (Pharmacia Discovery Research (Pfizer Global Research and Development), 700 Chesterfield Parkway West, Chesterfield, Missouri 63017-1732, USA.) Journal of medicinal chemistry, (2003 May 22) 46 (11) 2152-68. Journal code: 9716531. ISSN: 0022-2623. Pub. country: United States. Language: English.
AB A novel series of substituted N-[3-(1,1,2,2-tetrafluoroethoxy)benzyl]-N-(3-phenoxyphenyl)-trifluoro-3-amino-2-propanols is described which potently and reversibly inhibit **cholesteryl ester transfer protein** (**CETP**). Starting from the initial lead 1, various substituents were introduced into the 3-phenoxyaniline group to optimize the relative activity for inhibition of the **CETP**-mediated transfer of [3H]-cholesteryl ester from **HDL** donor particles to **LDL** acceptor particles either in buffer or in **human** serum. The better inhibitors in the buffer assay clustered among compounds in which the phenoxy group was substituted at the 3, 4, or 5 positions. In general, small lipophilic alkyl, haloalkyl, haloalkoxy, and halogen moieties increased potency relative to 1, while analogues containing electron-donating or hydrogen bond accepting groups exhibited lower potency. Compounds with polar or strong electron-withdrawing groups also displayed lower potency. Replacement of the phenoxy ring in 1 with either simple aliphatic or cycloalkyl ethers as well as basic heteroaryloxy groups led to reduced potency. From the better compounds, a representative series 4a-i was prepared as the chirally pure R(+) enantiomers, and from these, the 4-chloro-3-ethylphenoxy analogue was identified as a potent inhibitor of **CETP** activity in buffer (4a, IC50 0.77 nM, 59 nM in **human** serum). The simple R(+) enantiomer 4a represents the most potent acyclic **CETP** inhibitor reported. The chiral synthesis and biochemical characterization of 4a are reported along with its preliminary pharmacological assessment in animals.

L8 ANSWER 9 OF 44 MEDLINE on STN
2003247888. PubMed ID: 12771320. The **human cholesteryl ester transfer protein** I405V polymorphism is associated with plasma cholesterol concentration and its reduction by dietary phytosterol esters. Lottenberg Ana M; Nunes Valeria S; Nakandakare Edna R; Neves Monica; Bernik Marcia; Lagrost Laurent; dos Santos Jose E; Quintao Eder. (Lipid Laboratory (LIM10), University of Sao Paulo Medical School, Sao Paulo, Brazil.. lipideq@usp.br) . Journal of nutrition, (2003 Jun) 133 (6) 1800-5. Journal code: 0404243. ISSN: 0022-3166. Pub. country: United States. Language: English.
AB We examined the relationships of I405V **cholesteryl ester transfer protein** (**CETP**), TaqIB **CETP** and apolipoprotein (apo)E polymorphisms with the pattern of response to dietary plant sterol ester (PSE) by plasma lipids and **CETP** concentrations as well as lecithin-cholesterol acyltransferase (LCAT) activity. Subjects with moderate primary hypercholesterolemia (20-60 y old; 50 women; 10 men) consumed margarine (20 g/d) without (placebo) or with PSE (2.8 g/d = 1.68 g/d phytosterols) for 4 wk each period, in a crossover, double-blind study. Plasma **CETP** concentration was measured by ELISA; endogenous LCAT activity was expressed as the percentage of esterification (30 min incubation) of the subjects' (14)C-unesterified cholesterol **HDL**. PSE reduced concentrations of plasma total cholesterol (TC) (10%) and **LDL** cholesterol (

LDL-C) (12%). In relation to the I405V **CETP** polymorphism, the percentage reductions in TC with consumption of PSE for the II, IV and VV phenotypes were 7.2, 4.2 and not significant, respectively, whereas **LDL**-C significant reductions occurred only for II (9.5%). However, the **CETP** concentration diminished only in the II phenotype.

L8 ANSWER 10 OF 44 MEDLINE on STN

2003564888. PubMed ID: 14642415. Modulation of **HDL** metabolism by probucol in complete **cholesteryl ester transfer protein** deficiency. Noto Hiroshi; Kawamura Mitsunobu; Hashimoto Yoshiaki; Satoh Hiroaki; Hara Masumi; Iso-o Naoyuki; Togo Masako; Kimura Satoshi; Tsukamoto Kazuhisa. (Department of Metabolic Diseases, Graduate School of Medicine, University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-8655, Japan.) Atherosclerosis, (2003 Nov) 171 (1) 131-6. Journal code: 0242543. ISSN: 0021-9150. Pub. country: Ireland. Language: English.

AB Probucol, an antioxidative and hypolipidemic agent, has been postulated to increase reverse cholesterol transport by enhancing **cholesteryl ester transfer protein** (**CETP**) activity. However, its clinical implication in **CETP** deficient patients has not been fully defined. To characterize the effects of probucol in the absence of **CETP**, we evaluated the changes in lipid profile, lipid peroxidation, and paraoxonase 1 (PON1) activity in two complete **CETP** deficient patients, caused by treatment with probucol.When the patients were not receiving probucol, low-density lipoprotein (**LDL**) particles were smaller and high-density lipoprotein (**HDL**) particles were larger in these patients than in controls. Treatment with probucol (500 mg/day) resulted in the decrease in the levels of **HDL**-C and apolipoprotein (apo) A-I up to 22%. The size of **HDL** particles became smaller. **LDL** cholesterol concentration did not change in one patient, while it decreased by 47% in the other. PON1 activity/**HDL**-C, which was about 40% lower in the patients before treatment than in controls with the matching PON1 genotype, increased by 30% during the treatment. Lag time for **LDL** and **HDL** in both cases became prolonged more than 1.8 times after **administration** of probucol.This study demonstrated for the first time that probucol reduces **HDL**-C even in **humans** with complete **CETP** deficiency. Probucol treatment in these patients was also associated with protection of lipoproteins against oxidative stress, suggesting a clinical benefit of this drug even in such a state.

L8 ANSWER 11 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

2002174839 EMBASE Enhancement of cholesteryl ester transfer in plasma by hormone-replacement therapy. Ritsch A.; Kaser S.; Volgger B.; Abfalter E.; Sturm W.; Ganzer H.; Foger B.; Kirchmair R.; Ebenbichler C.; Patsch J.R.. Dr. J.R. Patsch, Department of Medicine, University of Innsbruck, Anichstr. 35, A-6020 Innsbruck, Austria. Metabolism: Clinical and Experimental Vol. 51, No. 5, pp. 599-604 2002.
Refs: 46.
ISSN: 0026-0495. CODEN: METAAJ
Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 20020530

AB To study possible mechanisms for the suggested protective effect of hormone-replacement therapy (HRT) with respect to cardiovascular disease we investigated lipoprotein parameters, mass and activity of lipoprotein-metabolizing enzymes, magnitude of postprandial lipemia, and vascular endothelial function in 13 postmenopausal women. All patients were examined before and 3 months after implementation of HRT with estrogen alone (group A, n = 6) or estrogen plus gestagen (group B, n = 7). HRT (groups A and B) resulted in enhanced total transfer of cholesteryl ester (CE) from higher-density lipoprotein (**HDL**) to apolipoprotein B (apoB)-containing lipoproteins (56% ± 11.45% v 50.82%

± 13.68%, P < .05) and increased apoA-I plasma concentration (171 ± 30 v 147 ± 22 mg/dL, P < .05). Fasting triglycerides (TG) were increased (134 ± 40 v 115 ± 39 mg/dL, P < .05). In group A patients the magnitude of postprandial lipemia increased significantly (1,737 ± 756 v 1,475 ± 930 mg TG/dL plasma/8 h, P < .05) without any change in lipoprotein lipase (LPL) activity, but with a concomitant decrease in low-density lipoprotein (**LDL**) size. In both groups flow-mediated dilation (FMD) reflecting vascular endothelial function was not influenced, suggesting that HRT may not directly affect vascular function but rather alters lipoprotein metabolism. The increase of apoA-I was not accompanied by an equivalent rise of **HDL** cholesterol. Based on the present data this finding can be readily explained by an increase in CE transfer from **HDL** to TG-rich lipoproteins, which is not due to increased **cholesteryl ester transfer protein** (**CETP**) plasma levels, but rather reflects an increase in fasting and postprandial TG. In conclusion, the net effect of accelerated CE transfer due to HRT depends on the balance of proatherogenic aspects, like the generation of small dense **LDL**, and antiatherogenic aspects, like the stimulation of reverse cholesterol transport.

L8 ANSWER 12 OF 44 MEDLINE on STN

2002650033. PubMed ID: 12409629. Effect of HMG-CoA reductase inhibitor on plasma **cholesteryl ester transfer protein** activity in primary hypercholesterolemia: comparison among **CETP**/TaqIB genotype subgroups. Kotake Hidetoshi; Sekikawa Akihiro; Tokita Yoshihisa; Ishigaki Yasushi; Oikawa Shinichi. (Division of Endocrinology and Metabolism, Tohoku University School of Medicine, Miyagi, Japan.) Journal of atherosclerosis and thrombosis, (2002) 9 (5) 207-12. Journal code: 9506298. ISSN: 1340-3478. Pub. country: Japan. Language: English.

AB We investigated the effects of HMG-CoA reductase inhibitors (statins) on the activity and concentration of plasma cholesterol ester transfer protein (**CETP**) in 30 hypercholesterolemic patients.Patients were divided into three groups according to TaqIB polymorphism of the **CETP** gene.The activity (158 +/- 23% control, mean +/- SEM) and concentration (4.1 +/- 1.0 mg/l) of plasma **CETP** were significantly ($p < 0.005$) higher in the subjects with the B1B1 genotype than B2B2 genotype (106 +/- 25% and 2.5 +/- 1.1 mg/l, respectively).Plasma **CETP** activity and concentration levels in the B1B2 group were intermediate between those of the B1B1 and B2B2 groups, and significantly ($p < 0.05$) low compared with the B1B1 group.Both the activity and concentration of plasma **CETP** were positively correlated with the **LDL**-cholesterol concentration ($r = 0.608$, $p < 0.0005$ and $r = 0.552$, $p < 0.005$, respectively).The **administration** of statins significantly reduced not only the activity ($p < 0.01$) but also the concentration ($p < 0.05$) of plasma **CETP** in hypercholesterolemic patients. Taken together, we confirmed that statins would be effective in increasing **HDL** levels in Japanese B1B1 carriers, because of a lower concentration of **HDL** cholesterol and higher level of plasma **CETP** compared to the other genotypes.The genetic variation in the **CETP** gene may be one important factor in designing better treatments.

L8 ANSWER 13 OF 44 EMBASE on STN

2001404056 EMBASE Novel agents for managing dyslipidaemia. Best J.D.; Jenkins A.J.. J.D. Best, University of Melbourne, Department of Medicine, St Vincent's Hospital Melbourne, Melbourne, Vic. 3065, Australia. jdbest@unimelb.edu.au. Expert Opinion on Investigational Drugs Vol. 10, No. 11, pp. 1901-1911 2001.
Refs: 100.
ISSN: 1354-3784. CODEN: EOIDER
Pub. Country: United Kingdom. Language: English. Summary Language:

English.
ED Entered STN: 20011206
AB An elevated low-density lipoprotein (**LDL**) cholesterol level is a strong predictor of coronary heart disease (CHD) risk. Over the past seven years, equally strong evidence has accumulated that lowering **LDL** cholesterol with HMG-CoA reductase inhibitors or statins reduces CHD risk and there is now widespread use of these agents for the primary and secondary prevention of CHD. Treatment issues remain regarding the appropriate degree of **LDL** cholesterol reduction and whether, in people with very high levels, it would be preferable to achieve the **LDL** cholesterol goal with a powerful statin alone or combined with an agent that lowers **LDL** cholesterol by a different mechanism. The main focus in the development of novel agents is the patient with low high-density lipoprotein (**HDL**) cholesterol, usually associated with hypertriglyceridaemia. Already prevalent as a risk factor for CHD, this abnormality has been linked with insulin resistance, which is likely to increase greatly over the next decade, along with increasing obesity and diabetes. Agents that have potent **HDL** cholesterol raising capacity include **cholesteryl ester transfer protein** (**CETP**) inhibitors, retinoid X receptor (RXR) selective agonists, specific peroxisome proliferator-activated receptor (PPAR) agonists and oestrogen-like compounds. Another area of development involves agents that will lower both cholesterol and triglyceride levels, such as partial inhibitors of microsomal triglyceride transfer protein (MTP) and perhaps squalene synthase inhibitors and agonists of AMP kinase. Future emphasis will be on correcting all lipid abnormalities for the prevention of CHD, not just lowering **LDL** cholesterol.

L8 ANSWER 14 OF 44 MEDLINE on STN
2000482102. PubMed ID: 10978256. Vaccine-induced antibodies inhibit **CETP** activity in vivo and reduce aortic lesions in a rabbit model of atherosclerosis. Rittershaus C W; Miller D P; Thomas L J; Picard M D; Honan C M; Emmett C D; Pettey C L; Adari H; Hammond R A; Beattie D T; Callow A D; Marsh H C; Ryan U S. (AVANT Immunotherapeutics, Inc, Needham, MA 02494, USA.. crittershaus@avantimmune.com) . Arteriosclerosis, thrombosis, and vascular biology, (2000 Sep) 20 (9) 2106-12. Journal code: 9505803. ISSN: 1524-4636. Pub. country: United States. Language: English.
AB Using a vaccine approach, we immunized New Zealand White rabbits with a peptide containing a region of **cholesteryl ester transfer protein** (**CETP**) known to be required for neutral lipid transfer function. These rabbits had significantly reduced plasma **CETP** activity and an altered lipoprotein profile. In a cholesterol-fed rabbit model of atherosclerosis, the fraction of plasma cholesterol in **HDL** was 42% higher and the fraction of plasma cholesterol in **LDL** was 24% lower in the **CETP** -vaccinated group than in the control-vaccinated group. Moreover, the percentage of the aorta surface exhibiting atherosclerotic lesion was 39.6% smaller in the **CETP**-vaccinated rabbits than in controls. The data reported here demonstrate that **CETP** activity can be reduced in vivo by vaccination with a peptide derived from **CETP** and support the concept that inhibition of **CETP** activity in vivo can be antiatherogenic. In addition, these studies suggest that vaccination against a self-antigen is a viable therapeutic strategy for disease management.

L8 ANSWER 15 OF 44 EMBASE
on STN
2001052571 EMBASE Low plasma lecithin:cholesterol acyltransferase and lipid transfer protein activities in growth hormone deficient and acromegalic men: Role in altered high density lipoproteins. Beentjes J.A.M.; Van Tol A.; Sluiter W.J.; Dullaart R.P.F.. R.P.F. Dullaart, Department of Endocrinology, University Hospital Groningen, PO Box 30 001, 9700 RB Groningen, Netherlands. e.maris@int.azg.nl. Atherosclerosis Vol. 153, No.

2, pp. 491-498 2000.
Refs: 61.
ISSN: 0021-9150. CODEN: ATHSBL
S 0021-9150(00)00433-0. Pub. Country: Ireland. Language: English. Summary Language: English.
ED Entered STN: 20010316
AB Growth hormone (GH) deficiency and acromegaly may be associated with increased cardiovascular risk. Little is known about alterations in high density lipoproteins (**HDL**) in these conditions. Lecithin:cholesterol acyl transferase (LCAT) has the ability to esterify free cholesterol (FC) in **HDL**. **Cholesteryl ester transfer protein** (**CETP**) is able to transfer cholesteryl esters (CE) from **HDL** to very low and low density lipoproteins (VLDL and **LDL**). During phospholipid transfer protein (PLTP) -mediated **HDL** remodelling, small pre β- **HDL** particles are generated which serve as acceptors for cellular cholesterol and provide the initial LCAT-substrate. We documented plasma lipids, LCAT, **CETP** and PLTP activity levels as well as plasma cholesterol esterification (EST) and cholesteryl ester transfer (CET) in 12 adult men with acquired GH deficiency, 12 acromegalic men and 24 healthy male subjects. All GH deficient and acromegalic patients received conventional hormonal replacement therapy if necessary. VLDL + **LDL** cholesterol and plasma triglycerides were higher in GH deficient ($P < 0.01$ and $P < 0.05$) and acromegalic patients ($P < 0.05$ and $P < 0.01$) than in healthy subjects. **HDL** cholesterol and **HDL** CE were lower ($P < 0.05$ for both) and the **HDL** FC/CE ratio was higher ($P < 0.01$) in these patient groups compared to healthy subjects. Plasma LCAT, **CETP** and PLTP activity levels were lower in acromegalic patients ($P < 0.01$ for all) and **CETP** activity was lower in GH deficient patients ($P < 0.01$) compared to healthy subjects. Plasma EST and CET were decreased in both acromegalic ($P < 0.01$ for both) and GH deficient patients ($P < 0.05$ for both). Multiple regression analysis demonstrated independent negative relationships of plasma insulin-like growth factor I with plasma LCAT ($P = 0.0001$), **CETP** ($P = 0.009$) and PLTP activity levels ($P = 0.021$). Plasma LCAT ($P = 0.0001$) and **CETP** activity ($P = 0.0001$) were also negatively associated with (substitution therapy for) adrenal insufficiency. In conclusion, GH deficient and acromegalic patients show abnormalities in **HDL**, consistent with impaired LCAT action. Decreases in plasma EST and CET in such patients, as well as a low PLTP activity in acromegaly suggest that reverse cholesterol transport may be impaired, contributing to increased cardiovascular risk.

L8 ANSWER 16 OF 44 EMBASE
on STN
2000257875 EMBASE A **cholesteryl ester transfer protein** inhibitor attenuate atherosclerosis in rabbits. Okamoto H.; Yonemori F.; Wakitani K.; Minowa T.; Maeda K.; Shinkal H.. H. Okamoto, Biological/Pharmacological Res. Lab., Central Pharmaceut. Res. Institute, JT Inc., 1-1 Murasaki-cho, Takatsuki, Osaka 569-1125, Japan. ye6h-okmt@asahi-net.or.jp. Nature Vol. 406, No. 6792, pp. 203-207 13 Jul 2000.
Refs: 28.
ISSN: 0028-0836. CODEN: NATUAS
Pub. Country: United Kingdom. Language: English. Summary Language: English.
ED Entered STN: 20000810
AB **Cholesteryl ester transfer protein** (**CETP**) is a plasma protein that mediates the exchange of cholesteryl ester in high-density lipoprotein (**HDL**) for triglyceride in very low density lipoprotein (VLDL). This process decreases the level of anti-atherogenic **HDL** cholesterol and increases pro- atherogenic VLDL and low density lipoprotein (**LDL**) cholesterol, so **CETP** is potentially atherogenic. On the other

hand, **CETP** could also be anti- atherogenic, because it participates in reverse cholesterol transport (transfer of cholesterol from peripheral cells through the plasma to the liver). Because the role of **CETP** in atherosclerosis remains unclear, we have attempted to develop a potent and specific **CETP** inhibitor. Here we describe **CETP** inhibitors that form a disulphide bond with **CETP**, and present one such inhibitor (JTT-705) that increases **HDL** cholesterol, decreases non-**HDL** cholesterol and inhibits the progression of atherosclerosis in rabbits. Our findings indicate that **CETP** may be atherogenic in vivo and that JTT-705 may be a potential anti-atherogenic drug.

L8 ANSWER 17 OF 44 MEDLINE on STN

1999353426. PubMed ID: 10426383. Plasma phospholipid transfer protein activity is lowered by 24-h insulin and acipimox **administration**: blunted response to insulin in type 2 diabetic patients. Riemens S C; van Tol A; Sluiter W J; Dullaart R P. (Department of Endocrinology, University Hospital Groningen, The Netherlands.) Diabetes, (1999 Aug) 48 (8) 1631-7. Journal code: 0372763. ISSN: 0012-1797. Pub. country: United States. Language: English.

AB **Cholesteryl ester transfer protein** (**CETP**) transfers cholesteryl esters from **HDL** to VLDL and **LDL**. Phospholipid transfer protein (PLTP) transfers phospholipids between lipoproteins, converts HDL3 into larger and smaller particles, and is involved in pre-beta-**HDL** generation. We examined the effects of 24-h hyperinsulinemia (30 mU x kg(-1) x h(-1)) and 24-h Acipimox (250 mg/4 h) on plasma lipids as well as **CETP** and PLTP activities (measured with exogenous substrate assays) in eight healthy and eight type 2 diabetic subjects. After 24 h of insulin, plasma free fatty acids (FFAs), **HDL** cholesterol, and plasma apolipoprotein AI decreased in healthy subjects and type 2 diabetic patients ($P < 0.05$). Plasma triglycerides did not significantly change in either group. After 24 h of Acipimox, all parameters, including plasma triglycerides, decreased in both groups ($P < 0.05$). Insulin decreased plasma PLTP activity by 17.6% after 24 h in healthy subjects ($P < 0.05$) and 10.2% in diabetic patients ($P < 0.05$ vs. baseline; $P < 0.05$ vs. healthy subjects). Acipimox lowered PLTP activity by 10.3% in healthy subjects ($P < 0.05$) and 11.3% in diabetic patients ($P < 0.05$). When insulin was infused for 3 h after Acipimox, a further decrease was found only in healthy subjects. Plasma **CETP** activity decreased by 9.5% after 24 h of insulin in healthy subjects ($P < 0.05$), but not in diabetic patients. Acipimox did not decrease plasma **CETP** activity in either group. In healthy subjects, the PLTP responses with insulin and Acipimox were larger than the changes in **CETP** activity ($P < 0.05$). These findings suggest that there is a metabolic link between the regulation of plasma FFA and PLTP, but not **CETP** . The PLTP response to insulin is blunted in type 2 diabetes.

L8 ANSWER 18 OF 44 MEDLINE on STN

1999293098. PubMed ID: 10364078. Estrogen-mediated increases in **LDL** cholesterol and foam cell-containing lesions in **human** ApoB100xCETP transgenic mice. Zuckerman S H; Evans G F; Schelm J A; Eacho P I; Sandusky G. (Division of Cardiovascular Research, Lilly Research Labs, DC0434, Indianapolis, Ind 46285, USA.. Zuckerman_Steven@Lilly.com) . Arteriosclerosis, thrombosis, and vascular biology, (1999 Jun) 19 (6) 1476-83. Journal code: 9505803. ISSN: 1079-5642. Pub. country: United States. Language: English.

AB The murine double transgenic mouse expressing both **human** apoB100 and **cholesteryl ester transfer protein** (**CETP**), has been used as a model to understand the effects mediated by various therapeutic modalities on serum lipoproteins and on atherosclerotic lesion progression. In the present study the effects of estrogen therapy on serum lipoproteins were investigated after mice were placed on an atherosclerotic diet. The daily oral **administration** of 20 or 100 microg/kg of 17 alpha-ethinyl

estradiol resulted in a significant, dose-dependent increase in **LDL** cholesterol over a 20-week regimen. These differences were apparent by 6 weeks and further increases were observed through the 20-week period. Although **CETP** did result in a reduction in total **HDL**, estrogen did not have any impact on the amount of **CETP** activity associated with the **HDL** particles. The significant increase in **LDL** cholesterol was associated with increases in the amount of apoB100 and B48 and apoE-containing particles. Hepatic apoB message levels, however, were not different between the experimental groups. Although the extent of atherosclerotic lesions was modest, <0.5% of the aortic surface area in the vehicle group, the high-dose estrogen group, showed an increase in lesion area consistent with the elevation in **LDL** cholesterol. These lesions, primarily restricted to the aortic root and aortic semilunar valves, were more intensely stained with Oil Red O in the high-dose estrogen group when compared with the vehicle controls.

L8 ANSWER 19 OF 44 EMBASE
on STN

1999206504 EMBASE Combined effects of probucol and bezafibrate on lipoprotein metabolism and liver **cholesteryl ester transfer protein** mRNA in cholesterol-fed rabbits. Ou J.; Saku K.; Jimi S.; Liao Y.-L.; Ohta T.; Zhang B.; Arakawa K.. Dr. K. Saku, Department of Internal Medicine, Fukuoka Univ. School of Medicine, 45-1-7 Nanakuma, Jonanku, Fukuoka 814-0180, Japan. hh035399@msat.fukuoka-u.ac.jp.
Japanese Circulation Journal Vol. 63, No. 6, pp. 471-477 1999.
Refs: 39.
ISSN: 0047-1828. CODEN: JCIRA2
Pub. Country: Japan. Language: English. Summary Language: English.

ED Entered STN: 19990701

AB Probucol decreases and bezafibrate increases plasma high density lipoprotein-cholesterol (**HDL**-C) levels in **humans.** This study was performed to determine whether the **HDL**-C-lowering effects of probucol could be reversed by treatment with bezafibrate in hypercholesterolemic rabbits. Forty-nine normolipidemic Japanese White rabbits were divided into 5 groups [group 1: normal chow; group 2: 0.2% cholesterol (Ch) diet; group 3: 0.2% Ch and 1% probucol diet; group 4: 0.2% Ch and 1% bezafibrate diet; group 5: 0.2% Ch and 1% probucol plus 1% bezafibrate diet] and treated for 8 weeks. Plasma lipids, **cholesteryl ester transfer protein** (**CETP**) activity in the lipoprotein- deficient plasma fraction, **CETP** mRNA in liver tissue and plasma drug concentrations were investigated. Serum total cholesterol (TC) increased after the rabbits in groups 2, 3, 4 and 5 were fed Ch, but overall, no significant differences were observed in serum TC and triglyceride (TG) among these groups. Serum **HDL**-C levels increased ($p<0.01$) in the bezafibrate- treated group, but a significant ($p<0.05$) reduction in **HDL**-C was observed in both the Ch + probucol (group 3) and Ch + probucol plus bezafibrate (group 5) groups; no significant difference was observed between groups 3 and 5. Significant correlation ($p<0.01$) was found between serum low density lipoprotein cholesterol (**LDL**-C) levels and plasma probucol concentrations in groups 3 and 5, but no correlation was found between plasma concentrations of probucol/bezafibrate and serum **HDL**-C levels. **CETP** activity in the lipoprotein-deficient plasma fraction increased in the Ch-, Ch + probucol-, and Ch + probucol and bezafibrate-fed groups (groups 2, 3 and 5, respectively), whereas a significant reduction in this activity was observed in the Ch + bezafibrate-fed group (group 4). An analysis of covariance showed that the **CETP** activity responded more sensitively to drug treatment than did the serum **HDL**-C level. **CETP** mRNA in liver tissue was assessed by Northern blotting at 8 weeks, but no changes were observed among the 5 groups. Probucol decreased and bezafibrate increased serum **HDL**-C levels, through **CETP** activity without affecting liver **CETP** mRNA levels, and the decrease in **HDL**-C levels produced by probucol could not be reversed by

bezafibrate.

L8 ANSWER 20 OF 44 MEDLINE on STN
1999231724. PubMed ID: 10217372. Plasma lipoprotein distribution and lipid transfer activities in patients with type IIb hyperlipidemia treated with simvastatin. Lagrost L; Athias A; Lemort N; Richard J L; Desrumaux C; Chatenet-Duchene L; Courtois M; Farnier M; Jacotot B; Braschi S; Gambert P. (Laboratoire de Biochimie des Lipoproteines, INSERM U498, Faculte de Medecine, Hopital du Bocage, Dijon, France.) Atherosclerosis, (1999 Apr) 143 (2) 415-25. Journal code: 0242543. ISSN: 0021-9150. Pub. country: Ireland. Language: English.

AB The aim of the present study was to search in type IIb hyperlipidemic patients for putative concomitant effects of simvastatin on the physicochemical characteristics of low density lipoproteins (**LDL**) and high density lipoproteins (**HDL**), as well as on the activities of the **cholesteryl ester transfer protein** (**CETP**) and the phospholipid transfer protein (PLTP) that were determined in both endogenous lipoprotein-dependent and endogenous lipoprotein-independent assays. In a double-blind, randomized trial, patients received either placebo (one tablet/day; n = 12) or simvastatin (20 mg/day; n = 12) for a period of 8 weeks after a 5-week run-in period. Simvastatin, unlike placebo, reduced the lipid and apolipoprotein B contents of the most abundant **LDL**-1, **LDL**-2, and **LDL**-3 subfractions without inducing significant changes in the overall size distribution of **LDL** and **HDL**. Whereas simvastatin significantly increased PLTP activity in an endogenous lipoprotein-dependent assay ($P < 0.01$), no variation was observed in a lipoprotein-independent assay. Simvastatin significantly decreased plasma **CETP** activity in an endogenous lipoprotein-dependent assay ($P < 0.01$), and the reduction in plasma cholesteryl ester transfer rates was explained by a 16% drop in **CETP** mass concentration ($P < 0.01$). In contrast, the specific activity of **CETP** was unaffected by the simvastatin treatment reflecting at least in part the lack of significant alteration in plasma triglyceride-rich lipoprotein acceptors. The simvastatin-induced changes in plasma **CETP** mass levels correlated positively with changes in plasma **CETP** activity ($r = 0.483$, $P = 0.0561$), in total cholesterol levels ($r = 0.769$; $P < 0.01$), and in **LDL**-cholesterol levels ($r = 0.736$; $P < 0.01$). Whereas the observations suggest that simvastatin might exert concomitant beneficial effects on plasma **CETP** and **LDL** levels, neither plasma cholesteryl ester transfer activity nor plasma phospholipid transfer activity appeared as the main determinants of the **LDL** and **HDL** distribution profiles in type IIb hyperlipidemic patients.

L8 ANSWER 21 OF 44 MEDLINE on STN
1999153462. PubMed ID: 10030391. Variations in serum cholesteryl ester transfer and phospholipid transfer activities in healthy women and men consuming diets enriched in lauric, palmitic or oleic acids. Lagrost L; Mensink R P; Guyard-Dangremont V; Temme E H; Desrumaux C; Athias A; Hornstra G; Gambert P. (Laboratoire de Biochimie des Lipoproteines, INSERM U498, Faculte de Medecine, Hopital du Bocage, Dijon, France.) Atherosclerosis, (1999 Feb) 142 (2) 395-402. Journal code: 0242543. ISSN: 0021-9150. Pub. country: Ireland. Language: English.

AB **Cholesteryl ester transfer protein** (**CETP**) and phospholipid transfer protein (PLTP) activities were measured in sera from 32 normolipidemic women and men consuming diets enriched in lauric, palmitic, or oleic acids. Serum **CETP** activity, measured as the rate of radiolabeled cholesteryl esters transferred from **HDL** toward serum apo B-containing lipoproteins, was higher with the palmitic acid diet (25.1+/-2.5%) than with the lauric acid (23.7+/-2.4%) and the oleic acid (24.0+/-2.7%) diets ($P = 0.0028$ and 0.0283, respectively). **CETP** mass concentrations, as measured with an enzyme-linked immunosorbent assay were increased after the lauric acid diet (2.57+/-0.63 mg/l) and the palmitic acid diet (2.49+/-0.64 mg/l)

as compared with the oleic acid diet (2.34+/-0.45 mg/l) (P = 0.0035 and 0.0249, respectively). In contrast with **CETP**, serum PLTP activity, as measured as the rate of radiolabeled phosphatidylcholine transferred from liposomes toward serum **HDL**, was significantly higher with the lauric acid diet (23.5+/2.6%) than with the palmitic acid diet (22.5+/-2.5%) (P = 0.0013), while no significant differences were noted when comparing the saturated diets versus the oleic acid diet (23.0+/-2.3%). No significant alterations in the mean apparent diameter of **LDL**, and in the relative proportions of individual **HDL** subpopulations were observed from one dietary period to another. Nevertheless, lipid transfer activities correlated significantly with the relative abundance of HDL2b, HDL2a, HDL3b, and HDL3c, with opposite tendencies being observed for cholesteryl ester transfer and phospholipid transfer activities. In general, serum **CETP** activity correlated negatively with **HDL** cholesterol, but positively with triglyceride concentrations after the dietary interventions, and the relations with serum lipids were just the opposite for PLTP activity. In addition, **CETP** and PLTP activities correlated negatively when subjects consumed the standardized diets (P < 0.05 in all cases), but not when subjects consumed their habitual diet. It is concluded that serum lipid transfer activities in normolipidemic subjects can be significantly affected by the fatty acid content of the diet, with differential effects on **CETP** and PLTP activities.

L8 ANSWER 22 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

1999179750 EMBASE Comparison of the effects of diet and simvastatin on serum high-density lipoprotein cholesterol and **cholesteryl ester transfer protein** activity in outpatients with hypercholesterolemia. Saito N.; Kannagi T.; Sayama H.. Dr. N. Saito, Internal Med./Adult Dis. Res. Dept., Miyazaki Aiwa Hospital, 2-16 Takamatsu-cho, Miyazaki, Miyazaki 880-0003, Japan. Current Therapeutic Research - Clinical and Experimental Vol. 60, No. 5, pp. 266-277 1999. Refs: 27.

ISSN: 0011-393X. CODEN: CTCEA

Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 19990610

AB We compared the effects of diet alone with those of diet plus simvastatin on serum lipids and lipoproteins, especially serum high-density lipoprotein cholesterol (**HDL**-C) and plasma **cholesteryl ester transfer protein** (**CETP**) activity, to determine whether these treatments affect the metabolism of **HDL**-C by **CETP**. A total of 27 outpatients (17 women and 10 men) with hypercholesterolemia (total cholesterol [TC] ≥220 mg/dL) were randomly assigned to treatment with diet (group D) or diet plus simvastatin 5 mg/d (group S). Serum TC and low-density lipoprotein cholesterol (**LDL**-C) decreased significantly in response to both diet and diet plus simvastatin treatment, although the reductions were significantly greater in group S than in group D (TC: 20% vs 13% [P < 0.05], **LDL**-C: 28% vs 18% [P < 0.01], respectively). Neither serum triglyceride (TG) levels nor percentage changes in TG differed significantly between the 2 groups. Serum **HDL**-C levels decreased in group D (P < 0.01) but increased in group S (P < 0.05). The serum TC:**HDL**-C and apolipoprotein B:A-I ratios decreased significantly in both groups (P < 0.05 and P < 0.01 in group D, and P < 0.0001 and P < 0.0001 in group S, respectively); the magnitude of the changes was greater in group S than in group D (P < 0.001, both ratios). Serum HDL2-C levels increased significantly only in group S (P < 0.05); HDL3-C, the HDL2-C:HDL3-C ratio, and **CETP** activity did not change significantly in either group. An inverse correlation between .DELTA.**CETP** and ΔHDL2-C was found in group D (r = -.550, P < 0.05); however, this correlation was not significant in group S. Simvastatin **administration**, which caused a significant reduction in both TC and **LDL**-C levels, did not produce a significant change in serum **CETP** activity. This is probably caused by the

inadequate decrease in TG levels or the maintenance of increased levels of **CETP**, during which TG-rich lipoproteins such as very- low-density lipoprotein and **LDL** act as acceptors for cholesteryl esters transferred from **HDL**-C by **CETP** activity.

L8 ANSWER 23 OF 44 MEDLINE on STN

1998376544. PubMed ID: 9710685. Effects of vitamin E and HMG-CoA reductase inhibition on **cholesteryl ester transfer protein** and lecithin-cholesterol acyltransferase in hypercholesterolemia. Napoli C; Leccese M; Palumbo G; de Nigris F; Chiariello P; Zuliani P; Somma P; Di Loreto M; De Matteis C; Cacciatore F; Abete P; Liguori A; Chiariello M; D'Armiento F P. (Department of Clinical and Experimental Medicine, University of Naples, Italy.) Coronary artery disease, (1998) 9 (5) 257-64. Journal code: 9011445. ISSN: 0954-6928. Pub. country: United States. Language: English.

AB BACKGROUND: The enzyme lecithin-cholesterol acyl transferase (LCAT) esterifies free cholesterol on high-density lipoprotein (**HDL**) and the **cholesteryl ester transfer protein** (**CETP**) transfers cholesteryl ester to very-low-density lipoprotein (VLDL) and low-density lipoproteins (**LDL**). Using statins, contradictory findings have been made regarding **CETP** activity in normolipidemic individuals and in those with familial dysbetalipoproteinemia. In contrast, LCAT activity appears to be unaffected by simvastatin. Antioxidants have also been proposed for the use of anti-atherosclerotic treatment, because the oxidation of **LDL** may have a key role in the pathophysiology of atherogenesis. OBJECTIVE: To investigate, in hypercholesterolemic patients, whether a combination of pravastatin with the antioxidant, vitamin E, has greater effects on the activity of **CETP** and of LCAT than does pravastatin alone. METHODS: This placebo-diet-controlled multicenter trial included 220 hypercholesterolemic patients who were assigned randomly to groups to receive: diet and 20-40 mg pravastatin (n = 52), diet and alpha-tocopherol (n = 60), or diet associated with placebo (n = 52). Plasma LCAT activity was determined using excess exogenous substrate, containing [3H]cholesterol. Plasma **CETP** activity was measured in the supernatant fraction after precipitation of endogenous apo B-containing lipoproteins with phosphotungstate-Mg2+. The exchange of cholesteryl esters between [14C]cholesteryl ester-labeled **LDL** and unlabeled **HDL** was measured during a 16-h incubation, while LCAT was inhibited. RESULTS: The addition of pravastatin to the diet induced a significant decrease in plasma **CETP** activity ($P < 0.05$); this effect was less evident in the group cotreated with vitamin E. For the first time, it was shown that **CETP** concentrations increased significantly after vitamin E alone ($P < 0.05$). No significant differences in the plasma activity of LCAT were observed among the groups. CONCLUSIONS: Pravastatin reduced **CETP** activity, but not that of LCAT. Addition of vitamin E prevented the decrease in **CETP** activity and had no effect on LCAT activity. The mechanism responsible for these effects is unknown, but could involve the prevention of radical-induced damage to **CETP** by vitamin E.

L8 ANSWER 24 OF 44 EMBASE on STN

1998064615 EMBASE Effects of testosterone replacement on **HDL** subfractions and apolipoprotein A-I containing lipoproteins. Tan K.C.B.; Shiu S.W.M.; Pang R.W.C.; Kung A.W.C.. Dr. K.C.B. Tan, Department of Medicine, Queen Mary Hospital, Pokfulam Road, Hong Kong, Hong Kong. Clinical Endocrinology Vol. 48, No. 2, pp. 187-194 1998. Refs: 41.
ISSN: 0300-0664. CODEN: CLENAO
Pub. Country: United Kingdom. Language: English. Summary Language: English.

ED Entered STN: 19980402

AB OBJECTIVES: Gonadal steroids are important regulators of lipoprotein metabolism. The aims of this study were to determine the effects of a

minimum effective dose of testosterone replacement on high density lipoprotein (**HDL**) subfractions and apolipoprotein (apo) A-I containing particles (lipoprotein (Lp)A-I) and LpA-I:A-II) in hypogonadal men with primary testicular failure and to investigate the underlying mechanisms of these changes. MEASUREMENTS: Eleven Chinese hypogonadal men were started on testosterone enanthate 250 mg intramuscularly at 4-weekly intervals. **HDL** was subfractionated by density gradient ultracentrifugation and LpA-I was analysed by electro- immunodiffusion after 3, 6 and 12 weeks of treatment. Plasma **cholesteryl ester transfer protein** (**CETP**) activity and lipolytic enzymes activities in post-heparin plasma were measured to determine the mechanisms underlying testosterone-induced changes in **HDL**. RESULTS: The dosage of testosterone enanthate used in the present study resulted in suboptimal trough testosterone levels. No changes were seen in plasma total cholesterol, triglyceride, low density lipoprotein cholesterol (**LDL**-C,) apo B and apo(a) after 12 weeks. There was a drop in HDL3-C compared to baseline (0.82 ± 0.17 mmol/1 vs. 0.93 ± 0.13, P< 0.01) whereas a small but significant increase was seen in HDL2-C (0.21 ± 0.13 mmol/vs. 0.11 ± 0.09, P<0.05). Plasma apo A-I decreased after treatment (1.34 ± 0.25 g/l vs. 1.50 ± 0.29, P<0.01), due to a reduction in LpA-I:A-II particles (0.86 ± 0.18 g/l vs. 0.99 ± 0.24, P<0.01). No changes were observed in the levels of LpA-I particles. No significant changes were seen in plasma **CETP** and lipoprotein lipase activities after testosterone replacement but there was a transient increase in hepatic lipase (HL) activity at weeks 3 and 6. The decrease in **HDL** correlated with the increase in HL activity (r= 0.62, P< 0.05). CONCLUSIONS: Testosterone replacement in the form of parenteral testosterone ester given 4-weekly, although unphysiological, was not associated with unfavourable changes in lipid profiles. The reduction in **HDL** was mainly in HDL3-C and in LpA-I:A-II particles and not in the more anti-atherogenic HDL2 and LpA-I particles. The changes in **HDL** subclasses were mainly mediated through the effect of testosterone on hepatic lipase activity.

L8 ANSWER 25 OF 44 MEDLINE on STN

1999079245. PubMed ID: 9863541. Cholesteryl ester transfer in hypercholesterolaemia: fasting and postprandial studies with and without pravastatin. Contacos C; Barter P J; Vrga L; Sullivan D R. (Department of Clinical Biochemistry, Royal Prince Alfred Hospital, New South Wales, Australia.) Atherosclerosis, (1998 Nov) 141 (1) 87-98. Journal code: 0242543. ISSN: 0021-9150. Pub. country: Ireland. Language: English.

AB Subjects with hypercholesterolaemia (HC) have increased fasting **cholesteryl ester transfer protein** (**CETP**) activity and accelerated cholesteryl ester transfer (CET) from **HDL** to apo B-containing lipoproteins. The aim of this study was to examine the effects of postprandial lipaemia and pravastatin treatment on plasma triglycerides (TG) and **CETP** activity and on CET and **LDL** Stokes' diameter in primary HC (n = 19, total cholesterol > or =6.5, **LDL**-cholesterol > or =4.5, TG <4.0 mmol/l). Samples were collected fasting and 6 h after an oral fat load (0.88 g/kg body weight) after 6 weeks therapy with placebo or pravastatin 40 mg nocte according to a double-blind randomized cross-over study. Apart from significant reductions in plasma total cholesterol, **LDL** -cholesterol apo B and TG. pravastatin significantly reduced **CETP** activity in both the fasting (mean +/- SD, 37.9+/-12.2 to 32.0+/-10.3 nmol/ml plasma per h) and postprandial state (35.5+/-11.3 to 31.3+/-9.5 nmol/ml plasma per h) compared to equivalent placebo phases. **CETP** activity did not change during postprandial lipaemia despite a significant 45-55% increase in CET to triglyceride-rich lipoproteins (TRL) of d <1.006 g/ml. **LDL** Stokes' diameter was unchanged postprandially or by pravastatin. The mass of TRL was the strongest contributor to variation in CET in both fasting and postprandial plasma, accounting for at least 77% of the variance of CET. Postprandial TRL-TG was the strongest contributor to variation in fasting **LDL** Stokes' diameter in

untreated HC (54%) whilst **HDL**-cholesterol was the strongest fasting contributor to variation (45%) for placebo- and pravastatin-treated HC. We conclude that pravastatin may reduce the atherogenicity of the lipoprotein profile in HC by reducing **CETP** activity. Furthermore, CET is strongly influenced by postprandial lipaemia which may have a cumulative effect on **LDL** size.

L8 ANSWER 26 OF 44 CAPLUS COPYRIGHT 2005 ACS on STN
1997:740308 Document No. 128:10315 Plasmid-based vaccine for treating atherosclerosis. Thomas, Lawrence J. (T Cell Sciences, Inc., USA). PCT Int. Appl. WO 9741227 A1 19971106, 66 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US7294 19970501. PRIORITY: US 1996-640713 19960501; US 1997-802967 19970221.

AB A plasmid-based vaccine is provided that is based on the combination of DNA segments coding for one or more B cell epitopes of **CETP** and one or more broad range helper T cell epitopes. **Administration** of the plasmids as a vaccine to a vertebrate subject provides an immune response to the subject's endogenous **CETP** and modulation of **CETP** activity, leading to prevention or reversal of various manifestations of heart disease. The vaccines provide an advantageous strategy for the prevention or treatment of atherosclerosis.

L8 ANSWER 27 OF 44 MEDLINE on STN
1998052393. PubMed ID: 9392500. **Cholesteryl ester transfer protein** gene polymorphism is a determinant of **HDL** cholesterol and of the lipoprotein response to a lipid-lowering diet in type 1 diabetes. Dullaart R P; Hoogenberg K; Riemens S C; Groener J E; van Tol A; Sluiter W J; Stulp B K. (Department of Endocrinology, University Hospital Groningen, The Netherlands.) Diabetes, (1997 Dec) 46 (12) 2082-7. Journal code: 0372763. ISSN: 0012-1797. Pub. country: United States. Language: English.

AB The TaqIB **cholesteryl ester transfer protein** (**CETP**) gene polymorphism (B1B2) is a determinant of **HDL** cholesterol in nondiabetic populations. Remarkably, this gene effect appears to be modified by environmental factors. We evaluated the effect of this polymorphism on **HDL** cholesterol levels and on the lipoprotein response to a linoleic acid-enriched, low-cholesterol diet in patients with type 1 diabetes. In 44 consecutive type 1 diabetic patients (35 men), **CETP** polymorphism, apolipoprotein (apo) E genotype, serum lipoproteins, serum **CETP** activity (measured with an exogenous substrate assay, n = 30), clinical variables, and a diet history were documented. The 1-year response to diet was assessed in 14 type 1 diabetic patients, including 6 B1B1 and 6 B1B2 individuals. **HDL** cholesterol was higher in 10 B2B2 than in 14 B1B1 homozygotes (1.63 +/- 0.38 vs. 1.24 +/- 0.23 mmol/l, P < 0.01). **HDL** cholesterol, adjusted for triglycerides and smoking, was 0.19 mmol/l higher for each B2 allele present. **CETP** activity levels were not significantly different between **CETP** genotypes. Multiple regression analysis showed that VLDL + **LDL** cholesterol was associated with dietary polyunsaturated:saturated fatty acids ratio (P < 0.02) and total fat intake (P < 0.05) in the B1B1 homozygotes only and tended to be related to the presence of the apo E4 allele (P < 0.10). In response to diet, VLDL + **LDL** cholesterol fell (P < 0.05) and **HDL** cholesterol remained unchanged in 6 B1B1 homozygotes. In contrast, VLDL + **LDL** cholesterol was unaltered and **HDL** cholesterol decreased (P < 0.05) in 6 B1B2 heterozygotes (P < 0.05 for difference in change in VLDL + **LDL**/**HDL** cholesterol ratio). This difference in response was unrelated to the apo E genotype. Thus, the TaqIB **CETP** gene polymorphism is a strong determinant

of **HDL** cholesterol in type 1 diabetes. This gene effect is unlikely to be explained by a major influence on the serum level of **CETP** activity, as an indirect measure of **CETP** mass. Our preliminary data suggest that this polymorphism may be a marker of the lipoprotein response to dietary intervention.

L8 ANSWER 28 OF 44 MEDLINE on STN

1998040278. PubMed ID: 9374122. Effect of 360His mutation in apolipoprotein A-IV on plasma **HDL**-cholesterol response to dietary fat. Jansen S; Lopez-Miranda J; Ordovas J M; Zambrana J L; Marin C; Ostos M A; Castro P; McPherson R; Lopez Segura F; Blanco A; Jimenez Pereperez J A; Perez-Jimenez F. (Lipid Research Unit, University Hospital Reina Sofia, University of Cordoba Medical School, Spain.) Journal of lipid research, (1997 Oct) 38 (10) 1995-2002. Journal code: 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB In order to determine whether genetic variability of apolipoprotein (apo) A-IV is responsible for the improvement in lipid profile when dietary saturated fats are replaced by carbohydrates or monounsaturated fats, 41 healthy male subjects were studied: 33 were homozygous for the 360Gln allele and 8 were heterozygote carriers of the 360His allele. These were administered three consecutive 4-week diets. The first was a diet rich in saturated fat (SAT diet, with 38% fat, 20% saturated. This was followed by a low fat diet (NCEP-I, with < 30% fat, < 10% saturated). The final diet was rich in monounsaturated fat (MUFA diet, with 38% fat, 22% monounsaturated). There was no difference in plasma lipid and apolipoprotein levels of both groups of individuals after consuming the SAT diet. Switching from this diet to the NCEP-I diet, carriers of the 360His allele presented a greater decrease in high density lipoprotein-cholesterol (**HDL**-C) (-10 vs. -1 mg/dL, P < 0.004) and apoA-I levels (-19 vs. -8 mg/dL, P < 0.037). Similarly, replacement of carbohydrates by monounsaturated fats produced a greater increase in **HDL**-C (9 vs. 1 mg/dL, P < 0.003) and apoA-I levels (9 vs. 2 mg/dL, P < 0.036) in carriers of the 360His mutation. Lecithin:cholesterol acyltransferase (LCAT) and **cholesteryl ester transfer protein** (**CETP**) activities and apoA-IV levels were also measured. However, no genotype-related differences were observed for these parameters. Our results suggest that variability in **HDL**-C and apoA-I response to diet is, at least partially, determined by the 360His mutation of apoA-IV.

L8 ANSWER 29 OF 44 MEDLINE on STN

97464110. PubMed ID: 9322801. Suppression of plasma **cholesteryl ester transfer protein** activity in acute hyperinsulinemia and effect of plasma nonesterified fatty acid. Arii K; Suehiro T; Yamamoto M; Ito H; Hashimoto K. (Second Department of Internal Medicine, Kochi Medical School, Japan.) Metabolism: clinical and experimental, (1997 Oct) 46 (10) 1166-70. Journal code: 0375267. ISSN: 0026-0495. Pub. country: United States. Language: English.

AB **Cholesteryl ester transfer protein** (**CETP**) is a major determinant of the plasma high-density lipoprotein cholesterol (**HDL**-C) level and plays an important role in the reverse cholesterol transport system. The purpose of this study was to determine the effect of acute hyperinsulinemia on plasma **CETP** activity in normal subjects and patients with non-insulin-dependent diabetes mellitus (NIDDM). Hyperinsulinemia was achieved using the hyperinsulinemic-euglycemic clamp. **CETP** activity was determined as the transfer of radiolabeled cholesterol in HDL3 to acceptor lipoprotein. Mean plasma **CETP** activity during an insulin infusion in both subject groups was significantly decreased compared with the mean basal activity. Suppression of plasma **CETP** activity in the NIDDM patients was significantly less than in the normal subjects (-4.2% +/- 7.9% v -9.6% +/- 6.4%, P < .02). Regression analysis showed that this suppression was correlated with plasma nonesterified fatty acid (NEFA) levels after the clamp and with the magnitude of the NEFA decrease (r = .318, P < .02 and r = .292, P < .05, respectively).

-mediated transfer of **HDL**-derived cholesteryl ester (CE) was the plasma triglyceride concentration, that is, the content of triglycerides per lipoprotein particle and the quantity of TG-containing particles (VLDL + **LDL**). In contrast, the fatty acid composition of these particles had less effect on **CETP**-mediated CE transfer.

L8 ANSWER 32 OF 44 MEDLINE on STN

96174676. PubMed ID: 8596480. Different effects of palmitic and stearic acid-enriched diets on serum lipids and lipoproteins and plasma **cholesteryl ester transfer protein** activity in healthy young women. Schwab U S; Maliranta H M; Sarkkinen E S; Savolainen M J; Kesaniemi Y A; Uusitupa M I. (Department of Clinical Nutrition, University of Kuopio, Finland.) Metabolism: clinical and experimental, (1996 Feb) 45 (2) 143-9. Journal code: 0375267. ISSN: 0026-0495. Pub. country: United States. Language: English.

AB The effects of palmitic and stearic acid-enriched diets on serum lipids, lipoproteins, apolipoproteins (apo) A-I and B, and plasma **cholesteryl ester transfer protein** (**CETP**) activity were examined in 12 healthy young women. Subjects followed the two experimental diets for 4 weeks according to a randomized crossover design. Both experimental diet periods were preceded by consumption of a baseline diet for 2 weeks. The diets provided 37% of total energy intake (E%) as fat, and differed only with respect to fatty acid composition. There was a substitution of 5E% of palmitic acid or stearic acid in the experimental diets for 5E% of monounsaturated fatty acids in the baseline diet. After the palmitic acid diet, serum total and high-density lipoprotein (**HDL**) cholesterol and apo A-I concentrations were higher (8%, P = .015, 9%, P = .040, and 11%,P = .011, respectively) and mean serum low-density lipoprotein (**LDL**) cholesterol concentration tended to be higher (8%, P = .077) as compared with values after the stearic acid diet. Plasma **CETP** activity increased in the palmitic acid diet as compared with the stearic acid diet (12%, P = .006). In conclusion, palmitic acid and stearic acid-enriched diets had different effects on serum lipids and lipoproteins and also on plasma **CETP** activity in young healthy women.

L8 ANSWER 33 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

96054122 EMBASE Document No.: 1996054122. Decrease in plasma **cholesteryl-ester transfer protein** activity with simvastatin treatment in patients with type IIa hypercholesterolemia. Hibino T.; Sakuma N.; Sato T.; Yoneyama A.; Fujinami T.. III Department of Internal Medicine, Nagoya City Univ. Medical School, Kawasumi-1, Mizuho-cho,Mizuho-Ku, Nagoya, Japan. Current Therapeutic Research - Clinical and Experimental Vol. 57, No. 1, pp. 42-47 1996. ISSN: 0011-393X. CODEN: CTCEA

Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 960312

AB We studied the effects of simvastatin treatment on plasma cholesterylester transfer protein (**CETP**) activity and lipid levels in patients with type IIa hypercholesterolemia. We treated 24 patients, 4 men and 20 women aged 49 to 81 years (mean age, 64.5 ± 8.5 years), with simvastatin at a daily dose of 5 mg for 4 weeks. Simvastatin treatment significantly decreased plasma total cholesterol (262 ± 28 mg/dL vs 220 ± 28 mg/dL) and low-density lipoprotein cholesterol (**LDL**-C) (181 ± 26 mg/dL vs 135 ± 28 mg/dL) and significantly increased high-density lipoprotein cholesterol (**HDL**-C) (57.2 ± 8.4 mg/dL vs 62.8 ± 10.5 mg/dL. **CETP** activity significantly decreased after 4 weeks of treatment (11.2 ± 3.8%/10 μL/3 h vs 8.9 ± 3.8%/10 μL/3 h. These results suggest that one of the lipid-lowering effects of simvastatin is due to decreased **CETP** activity, which results in decreased **LDL**-C and increased **HDL**-C concentrations.

L8 ANSWER 34 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on

The data suggest that acute hyperinsulinemia reduces plasma **CETP** activity through a decrease in plasma NEFA.

L8 ANSWER 30 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

97233635 EMBASE Document No.: 1997233635. Plasma **cholesteryl ester transfer protein** is lowered by treatment of hypercholesterolemia with cholestyramine. Carrilho A.J.F.; Medina W.L.; Nakandakare E.R.; Quintao E.C.R.. Dr. E.C.R. Quintao, Lipids Laboratory, LIM-10, Faculdade de Medicina da USP, Av. Dr. Arnaldo 455, s/3317, CEP 01246-903, Sao Paulo, Brazil. Clinical Pharmacology and Therapeutics Vol. 62, No. 1, pp. 82-88 1997.
Refs: 32.
ISSN: 0009-9236. CODEN: CLPTAT
Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 970822

AB Cholestyramine (INN, colestyramine) treatment of subjects with hypercholesterolemia reduced the plasma level of **cholesteryl ester transfer protein** (**CETP**) as measured by radioimmunoassay (**CETP**-RIA) and, as expected, also reduced the levels of total cholesterol, low-density lipoprotein (**LDL**) cholesterol, and apolipoprotein B. The extent of **CETP** variation was significant only in the subjects whose **LDL** cholesterol levels were reduced by more than 25%. Furthermore, **CETP**-RIA was correlated with total cholesterol, **LDL** cholesterol, and apolipoprotein B concentrations. Plasma **CETP** was also measured by an indirect procedure that uses high-density lipoprotein (**HDL**) 14C-cholesteryl ester and very low-density lipoprotein cholesterol from a pool of plasma donors, and the patient's plasma as the source of **CETP**. The two procedures for **CETP** determination correlated well with each other, although the **CETP**-RIA. was more sensitive in the detection of changes of plasma **CETP** ascribed to cholestyramine (INN, colestyramine) treatment. The rise of plasma **HDL** cholesterol levels after cholestyramine probably resulted from the reduction of **CETP** activity.

L8 ANSWER 31 OF 44 MEDLINE on STN

97057822. PubMed ID: 8902152. Plasma cholesteryl ester synthesis, **cholesteryl ester transfer protein** concentration and activity in hypercholesterolemic women: effects of the degree of saturation of dietary fatty acids in the fasting and postprandial states. Lottenberg A M; Nunes V S; Lottenberg S A; Shimabukuro A F; Carrilho A J; Malagutti S; Nakandakare E R; McPherson R; Quintao E C. (Division of Nutrition and Lipids Laboratory (LIM 10), Hospital of the University of Sao Paulo Medical School, Brazil.) Atherosclerosis, (1996 Oct 25) 126 (2) 265-75. Journal code: 0242543. ISSN: 0021-9150. Pub. country: Ireland. Language: English.

AB Hypercholesterolemic women (n = 19) sequentially maintained on a long-term saturated (SAT) or a polyunsaturated (PUFA) fatty acid-rich diet, respectively, were studied in the fasting state and after a meal rich in SAT or PUFA. When apo B-containing lipoprotein was excluded from plasma the in vitro **HDL**-14C-cholesterol esterification rate was identical for the saturated (SAT) and polyunsaturated (PUFA) fatty acid diets, and did not increase during the postprandial period. Rates of transfer of 14C-cholesteryl ester to apo B-containing lipoproteins from **HDL** were also similar for both diets in the fasting state and increased to the same extent in the postprandial period in parallel with the rise in plasma triglycerides. When transfer data were related to the plasma concentration of apo B, the gain of cholesteryl ester by the triglyceride-containing particles (VLDL + **LDL**) also increased in the postprandial period to a similar extent for both diets. **Cholesteryl ester transfer protein** (**CETP**) concentration measured by radioimmunoassay was similar during both experimental diets, although greater in the postprandial period for the PUFA diet. The rate limiting factor for **CETP**

STN

1995:489787 Document No.: PREV199598504087. Pravastatin modulates cholesteryl ester transfer from **HDL** to Apob-containing lipoproteins and lipoprotein subspecies profile in familial hypercholesterolemia. Guerin, Maryse [Reprint author]; Dolphin, Peter J.; Talussot, Corinne; Gardette, Jean; Berthezene, Francois; Chapman, M. John. INSERM U 321, Pavillion Benjamin Delessert, Hop. Pitie, 83 Boulevard Hop., 75651 Paris Cedex 13, France. Arteriosclerosis Thrombosis and Vascular Biology, (1995) Vol. 15, No. 9, pp. 1359-1368.
ISSN: 1079-5642. Language: English.

AB Familial hypercholesterolemia (FH) results from genetic defects in the **LDL** receptor, and is characterized by a marked elevation in plasma **LDL** and by qualitative abnormalities in **LDL** particles. Because **LDL** particles are major acceptors of cholesteryl esters (CEs) from **HDL**, significant changes occur in the flux of CE through the reverse cholesterol pathway. To evaluate the effects of an HMG-CoA reductase inhibitor, pravastatin, on CE transfer from **HDL** to apo B-containing lipoproteins and on plasma lipoprotein subspecies profile in subjects with heterozygous FH, we investigated the transfer of **HDL**-CE to **LDL** subtractions and changes in both concentration and chemical composition of the apo B- and the apo AI-containing lipoproteins. After pravastatin treatment (40 mg/d) for a 12-week period, plasma **LDL** concentrations (mean +- SD, 745.4+- 51.9 mg/dL) were reduced by 36% in patients with FH (n=6). By contrast, the qualitative features of the density profile of **LDL** subspecies in patients with FH, in whom the intermediate (d=1.029 to 1.039 g/mL) and dense (d=1.039 to 1.063 g/mL) subspecies were significantly increased relative to a control group, were not modified by pravastatin. In addition, no significant effect on the chemical composition of individual **LDL** subfractions was observed. Furthermore, plasma **HDL** concentrations were not modified, although the density distribution of **HDL** was normalized, Indeed, the **HDL** density peak was shifted towards the **HDL**-2 subfraction (ratios of **HDL**-2 to **HDL**-3 were 0.7 and 1.1 before and after treatment, respectively). Evaluation of plasma CE transfer protein (**CETP**) mass was performed with an exogenous CE transfer assay. Under these conditions, no modification of plasma **CETP** protein mass was induced by pravastatin **administration.** However, the rate of CE transfer from **HDL** to **LDL** was reduced by 24% by pravastatin (61 +- 17 mu-g CE cntdot h-1 cntdot mL-1 plasma; P lt .0005), although intermediate and dense **LDL** subtractions again accounted for the majority (71%) of the total CE transferred to **LDL.** Thus, pravastatin induced reduction of plasma **CETP** activity without change in the preferential targeting of the transfer of **HDL**-CE towards the denser **LDL** subtractions. In conclusion, pravastatin reduces the elevated flux of CE from **HDL** to apo B-containing lipoproteins in subjects with heterozygous FH as a result of a reduction in the **LDL** particle acceptor concentration.

L8 ANSWER 35 OF 44 EMBASE on STN

95134162 EMBASE Document No.: 1995134162. Accelerated cholesteryl ester transfer and altered lipoprotein composition in diabetic cynomolgus monkeys. Bagdade J.D.; Wagner J.D.; Rudel L.L.; Clarkson T.B.. Section of Endocrinology/Metabolism, Rush-Presbyterian-SLMC, 1653 West Congress Parkway,Chicago, IL 60612-3864, United States. Journal of Lipid Research Vol. 36, No. 4, pp. 759-766 1995.
ISSN: 0022-2275. CODEN: JLPRAW
Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 950516

AB To determine whether nonhuman primates demonstrate the same alterations in transport of cholesteryl ester (CE) in plasma observed in diabetic **humans**, cholesteryl ester transfer (CET) was measured in cynomolgus monkeys with chronic spontaneous diabetes mellitus (glycated

hemoglobin: diabetics 10.7 ± 4.1%; controls 3.8 ± 0.8%, P < 0.005). Among the plasma lipids, only triglycerides were significantly increased in diabetic monkeys (diabetics 303 ± 294 mg/dl; controls 85 ± 34 mg/dl; P < 0.05); total plasma, **LDL**, HDL2, and HDL3 cholesterol concentrations did not differ significantly from those of control animals. Similar to **human** beings with insulin-dependent and non-insulin-dependent diabetes mellitus, CET estimated both as the mass of cholesteryl ester transferred from **HDL** to the apoB containing lipoproteins (VLDL + **LDL**) and as the loss of radiolabeled cholesteryl ester from **HDL** was significantly greater (P < 0.001) in diabetic compared to control monkeys. Glycated hemoglobin levels in the combined control and diabetic groups correlated directly with both the mass of cholesteryl ester transferred at 2 h (r = 0.75; P < 0.001) and the isotopic transfer (k) (r = 0.64; P < 0.005). The mass of **cholesteryl ester transfer protein** (**CETP**) tended to be higher in the diabetic animals (diabetic 4.06 ± 0.73 μg/ml versus control 3.05 ± 0.93; P < 0.1). Consistent with CET being enhanced in vivo in the diabetic animals, compositional studies revealed that the triglyceride:cholesteryl ester core lipid ratio of their VLDL tended to be lower and **LDL** and HDL2 significantly higher than in controls (P < 0.001); and like **human** beings with noninsulin-dependent diabetes mellitus, the free cholesterol:lecithin ratio was reduced in their HDL2 (P < 0.05). Moreover, the sphingomyelin:lecithin ratio was significantly reduced in the diabetic monkeys' VLDL and **LDL** (P < 0.05 and P < 0.005, respectively), indicating that a disturbance also was present in lipoprotein surface phospholipid composition. Thus, diabetic cynomolgus monkeys have abnormalities in CET and disturbances in lipoprotein composition that resemble those in **human** beings with diabetes mellitus. Cynomolgus monkeys may be useful models for studying the mechanism(s) that underlie the acceleration of CET and altered lipoprotein composition in diabetic patients.

L8 ANSWER 36 OF 44 MEDLINE on STN

95105666. PubMed ID: 7806977. Inhibition of **cholesteryl ester transfer protein** in normocholesterolemic and hypercholesterolemic hamsters: effects on **HDL** subspecies, quantity, and apolipoprotein distribution. Evans G F; Bensch W R; Apelgren L D; Bailey D; Kauffman R F; Bumol T F; Zuckerman S H. (Division of Cardiovascular Research, Lilly Research Labs, Lilly Corporate Center, Indianapolis, IN 46285.) Journal of lipid research, (1994 Sep) 35 (9) 1634-45. Journal code: 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB The effects of **cholesteryl ester transfer protein** (**CETP**) inhibition on the serum lipoprotein profile in both normocholesterolemic and hypercholesterolemic hamsters has been determined following subcutaneous injection of 12.5 mg/kg of the **CETP** neutralizing monoclonal antibody, TP2. Inhibition of **CETP** activity was greater than 60% and resulted in a 30-40% increase in high density lipoprotein (**HDL**) in both normal and hypercholesterolemic animals. These **HDL** effects were observed 1 day post-injection, were maximal by 4 days, and returned to control values by 14 days. Inhibition of **CETP** activity resulted in a decrease in both low density lipoprotein (**LDL**) and very low density lipoprotein (VLDL) cholesterol concomitant with **HDL** increase, and in hypercholesterolemic animals resulted in increased total serum cholesterol. In addition to the quantitative differences in **LDL** and **HDL**, there were significant increases in the size of the **HDL**, a shift to smaller **LDL** particles, and changes in apolipoprotein (apo) composition as evaluated by FPLC and Western blot analysis. Large apoA-I-poor and apoE-containing **HDL** became prevalent in hypercholesterolemic hamsters after **CETP** inhibition. In addition, the size of the **CETP**-containing **HDL** particles increased with inhibition of transfer activity. While these effects were apparent in normocholesterolemic animals, the

changes in apolipoprotein distribution and **HDL** subspecies as detected on native gels were more significant in the hypercholesterolemic animals. The changes in the **HDL** profile and apolipoprotein distribution after **CETP** inhibition in hamsters were similar to those reported in **CETP**-deficient Japanese subjects, suggesting the utility of the hypercholesterolemic hamster as an in vivo model for the understanding of the lipoprotein changes associated with **CETP** inhibition.

L8 ANSWER 37 OF 44 CAPLUS COPYRIGHT 2005 ACS on STN
1994:188053 Document No. 120:188053 Exercise training decreases plasma **cholesteryl ester transfer protein.**
Seip, Richard L.; Moulin, Phillipe; Cocke, Thomas; Tall, Alan; Kohrt, Wendy M.; Mankowitz, Keith; Semenkovich, Clay F.; Ostlund, Richard; Schonfeld, Gustav (Sch. Med., Washington Univ., St Louis, MO, USA). Arteriosclerosis and Thrombosis, 13(9), 1359-67 (English) 1993. CODEN: ARTTE5. ISSN: 1049-8834.
AB To assess the effect of exercise on the plasma concentration of cholesterol ester transfer protein (**CETP**) and its possible influence in mediating the exercise-associated redistribution of cholesterol among plasma lipoproteins, the authors measured plasma **CETP** in 57 healthy normolipidemic men and women before and after 9 to 12 mo of exercise training. The training protocol resulted in significant changes in Vo2max (mean±SD, +5.3±3.5 mL.kg-1.min-1), body weight (-2.5±3.5 kg), plasma triglycerides (-25.7±36.3 mg/dL), high-d. lipoprotein cholesterol (**HDL**-C) (+2.6±6.2 mg/dL), and ratios of total cholesterol to **HDL**-C (-0.30±0.52) and low-d. lipoprotein cholesterol (**LDL**-C) to **HDL**-C (-0.18±0.45) (all P≤.05) but no change in lipoprotein(a). **CETP** concentration (in milligrams per L) fell significantly in response to training in both men (n=28, 2.47±0.66 to 2.12±0.43; % Δ=14.2%; P<.005) and women (n=29, 2.72±1.01 to 2.36±0.76; % Δ=13.2%; P<.047). The **CETP** change was observed both in subjects who lost weight (n=28, Δ mean weight=-5.0 kg; Δ **CETP**=-0.42±0.79; % Δ=15.4%; P<.009) and in those who were weight stable (n=29, Δ mean weight=-0.12 kg; Δ **CETP**=-0.29±0.78; % Δ=10.4%; P<.055). Pretraining plasma **CETP** concentration predicted training-associated changes in **HDL**-C (r=-.27, P<.04) and ratio of **LDL**-C to **HDL**-C (r=+.40, P<.002). In a smaller study of 15 men, exercise training was associated with a decrease in levels of **CETP**, an increase in plasma postheparin lipoprotein lipase (LPL) activity, and a decrease in hepatic triglyceride lipase (HTGL) activity. Overall, the data suggest that basal plasma **CETP** concns., in addition to LPL and HTGL activities, may contribute to determining the extent to which exercise redistributes cholesterol among plasma lipoproteins.

L8 ANSWER 38 OF 44 MEDLINE on STN
93224829. PubMed ID: 8468527. **Cholesteryl ester transfer protein** and high density lipoprotein responses to cholesterol feeding in men: relationship to apolipoprotein E genotype.
Martin L J; Connelly P W; Nancoo D; Wood N; Zhang Z J; Maguire G; Quinet E; Tall A R; Marcel Y L; McPherson R. (Lipoprotein and Atherosclerosis Group, McGill University, Canada.) Journal of lipid research, (1993 Mar) 34 (3) 437-46. Journal code: 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.
AB The apolipoprotein (apo) E isoform is an important determinant of the plasma lipoprotein distribution of apoE and of the metabolism of apoE-containing lipoproteins. We have determined the effects of apoE genotype on the plasma lipoprotein response to cholesterol feeding in 30 young normal male subjects (5 E3/2, 11 E3/3, 14 E4/3) under rigorously controlled dietary conditions. Two diets, differing only in cholesterol content (low cholesterol (LC): 80 mg cholesterol/1000 kcal and high cholesterol (HC): 320 mg cholesterol/1000 kcal), were compared using a random crossover design. At the end of the HC as compared to the LC

period, total cholesterol (TC), low density lipoprotein cholesterol (**LDL**-C), high density lipoprotein cholesterol (**HDL**-C), and HDL2-C increased by an average of 15%, 21%, 7%, and 23%, respectively, for the three genotype groups combined (P < 0.001 for each). The **LDL**-C response to dietary cholesterol did not differ among the apoE genotypes. However, the increase in **HDL**-C varied significantly according to the apoE genotype (E3/2: 0 change, E3/3: +4%, E4/3: +12%; P < 0.05). The plasma **cholesteryl ester transfer protein** (**CETP**) response to cholesterol feeding also differed amongst the three apoE genotype groups (E3/2: +37%, E3/3: +18%, E4/3: +9%) (P < 0.05). ApoE genotype has significant and opposite effects on plasma **CETP** and **HDL** -C responses to dietary cholesterol in men.

L8 ANSWER 39 OF 44 EMBASE on STN

93269750 EMBASE Document No.: 1993269750. Effects of pravastatin on apolipoprotein-specific high density lipoprotein subpopulations and low density lipoprotein subclass phenotypes in patients with primary hypercholesterolemia. Cheung M.C.; Austin M.A.; Moulin P.; Wolf A.C.; Cryer D.; Knopp R.H.. Northwest Lipid Research Lab., 2121 N. 35th Street,Seattle, WA 98103, United States. Atherosclerosis Vol. 102, No. 1, pp. 107-119 1993.
ISSN: 0021-9150. CODEN: ATHSBL
Pub. Country: Ireland. Language: English. Summary Language: English.

ED Entered STN: 931010

AB The HMG-CoA reductase inhibitor class of cholesterol-lowering agents reduces very low density lipoproteins (VLDL) and low density lipoproteins (**LDL**) and slightly increases high density lipoproteins (**HDL**). However, the effects of these agents on subclasses within the **LDL** and **HDL** fractions are not well understood. We have employed an HMC-CoA reductase inhibitor, pravastatin, to determine if **LDL** subclass phenotypes, as determined by gradient gel electrophoresis, and **HDL** particles containing both apolipoprotein (apo) A-I and A-II, Lp(AI w AII), and those containing apo A-I but not A-II, Lp(AI w/o AII) are affected by pravastatin (10 mg daily). Twenty-four subjects with **LDL**-cholesterol (**LDL** -C) > 160 mg/dl, triglyceride (TG) < 350 mg/dl and no recent myocardial infarction or secondary causes of hypercholesterolemia were enrolled. Compared with an age- and sex-matched normolipidemic reference group (controls), the hypercholesterolemic subjects had reduced levels of Lp(AI w/o AII) and increased levels of Lp(AI w AII) at baseline. In addition, both of their **HDL** subpopulations had significantly more small (7.0-8.2 nm) particles (P < 0.02 and 0.0001) but significantly fewer large (9.2-11.2 nm) particles (P < 0.002 and 0.0001). Pravastatin induced statistically significant (P < 0.001) reductions in plasma total C (15%), **LDL**-C (18%), and apo B (16%). While apo A-I and A-II levels increased 5% (P < 0.001) and 6% (P < 0.05), respectively, concentration, composition, and size abnormalities in Lp(AI w AII) and Lp(AI w/o AII) persisted. Lp(a), apo E and **cholesteryl ester transfer protein** (**CETP**) levels also did not change. Although changes in **LDL** subclass phenotypes were observed, all changes involved the intermediate phenotype, and no significant changes in **LDL** peak particle diameter were seen in either group. Interrelationships between **CETP**, **LDL** subclass phenotypes and **HDL** subpopulations were also seen. Conclusions: Although pravastatin decreased plasma apo B and **LDL** lipid concentrations, no major changes were seen in **LDL** subclass phenotypes or **HDL** subpopulations even in the presence of abnormalities associated with arteriosclerosis. Similarly, **CETP** , which is believed to play a role in **HDL** and **LDL** particle size distribution, did not change with pravastatin treatment. Further research is needed to determine the pathophysiological basis of abnormal **HDL** and **LDL** subclasses in hypercholesterolemia and explore methods of rectifying the abnormalities.

L8 ANSWER 40 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

93198044 EMBASE Document No.: 1993198044. Role of elevated lecithin: Cholesterol acyltransferase and **cholesteryl ester transfer protein** activities in abnormal lipoproteins from proteinuric patients. Dullaart R.P.F.; Gansevoort R.T.; Dikkeschei B.D.; De Zeeuw D.; De Jong P.E.; Van Tol A.. Department of Endocrinology, University Hospital, P.O. Box 30.001,9700 RB Groningen, Netherlands. Kidney International Vol. 44, No. 1, pp. 91-97 1993. ISSN: 0085-2538. CODEN: KDYIA5 Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 930808

AB Lecithin:cholesterol acyltransferase (LCAT) and **cholesteryl ester transfer protein** (**CETP**) are key factors in the esterification of free cholesterol, and the distribution of cholesteryl ester among lipoproteins in plasma. Alterations in these processes may play a role in the lipoprotein abnormalities associated with glomerular proteinuria. The activities of LCAT and **CETP** were measured using excess exogenous substrate assays in nine patients with nephrotic-range proteinuria and in 18 matched controls. The proteinuria-lowering effect of four weeks of angiotensin converting enzyme (ACE) inhibition with enalapril was also studied. Plasma very low lipoprotein and low density lipoprotein (VLDL and **LDL**) cholesterol; triacylglycerol and apolipoprotein B levels were significantly elevated in the patients compared with controls. High density lipoprotein (**HDL**) total cholesterol, free cholesterol, cholesteryl ester and the free cholesterol/cholesteryl ester ratio in **HDL** were lower. Total plasma apolipoprotein A1 was normal. Plasma LCAT and **CETP** activities were elevated in the patients by 30% ($P < 0.01$) and by 39% ($P < 0.01$), respectively, and were both inversely related to serum albumin. VLDL and **LDL** cholesterol levels were positively related to LCAT and **CETP** activities, whereas the **HDL** free cholesterol content was inversely related to LCAT activity. ACE inhibition resulted in a 40% reduction of proteinuria, a partial normalization of LCAT activity, and a decrease in VLDL and **LDL** cholesterol. In conclusion, elevated activities of LCAT and **CETP** may provide a mechanism that contributes to the low proportion of cholesterol in **HDL** relative to that in VLDL and **LDL**, as well as to the compositional changes of **HDL** seen in glomerular proteinuria. Such abnormalities could contribute to accelerated development of atherosclerosis in proteinuric states.

L8 ANSWER 41 OF 44 MEDLINE on STN

93002916. PubMed ID: 1390587. Effect of marine lipids on cholesteryl ester transfer and lipoprotein composition in patients with hypercholesterolemia. Bagdade J D; Ritter M C; Davidson M; Subbaiah P V. (Rush Medical College, Chicago, Ill.) Arteriosclerosis and thrombosis : a journal of vascular biology / American Heart Association, (1992 Oct) 12 (10) 1146-52. Journal code: 9101388. ISSN: 1049-8834. Pub. country: United States. Language: English.

AB While the effects of omega-3 (n-3) fatty acids present in marine lipids on plasma lipoprotein levels have been intensively studied, less is known about their impact on reverse cholesterol transport. For this reason, for a 3-month period we studied the effects of the **administration** of n-3 fatty acids (6 g/day) as a dietary supplement on cholesteryl ester transfer (CET), a key step in this process, and lipoprotein composition in 12 outpatients with genetically heterogeneous forms of hypercholesterolemia. Before treatment, CET in hypercholesterolemic patients, estimated as the mass of cholesteryl ester (CE) transferred from high density lipoprotein (**HDL**) to very low density lipoprotein (VLDL) plus low density lipoprotein (**LDL**), was markedly accelerated, peaking after only 1-2 hours of incubation of whole plasma; this response differed significantly ($p < 0.001$) from the initial delayed curvilinear response of control subjects. Consistent with the accelerated

CET occurring in vivo, their triglyceride to esterified cholesterol core lipid ratio before treatment was reduced in the intact VLDL fraction and VLDL1 but not in VLDL2 or VLDL3 and was reciprocally increased in **HDL**. In addition, the free (unesterified) cholesterol to lecithin ratio of VLDL1 was abnormally increased. Recombination experiments performed with individual lipoprotein fractions revealed that accelerated CET was specifically associated with the VLDL1 subfraction and not **LDL**, **HDL**, and **cholesteryl ester transfer protein** (**CETP**), although pretreatment levels of **CETP** were significantly increased ($p < 0.01$). (ABSTRACT TRUNCATED AT 250 WORDS)

L8 ANSWER 42 OF 44 MEDLINE on STN

93114969. PubMed ID: 1473909. Effects of purified eicosapentaenoic acid ethyl ester on plasma lipoproteins in primary hypercholesterolemia. Nozaki S; Matsuzawa Y; Hirano K; Sakai N; Kubo M; Tarui S. (Second Department of Internal Medicine, Osaka University Medical School, Fukushima, Japan.) International journal for vitamin and nutrition research. Internationale Zeitschrift fur Vitamin- und Ernahrungsforschung. Journal international de vitaminologie et de nutrition, (1992) 62 (3) 256-60. Journal code: 1273304. ISSN: 0300-9831. Pub. country: Switzerland. Language: English.

AB We investigated the effects of purified eicosapentaenoic acid (EPA) ethyl ester capsules (90% purity), which are free from cholesterol, saturated fatty acids and docosahexaenoic acid (DHA), on plasma lipoproteins and **cholesteryl ester transfer protein** (**CETP**) activity. We administered 2.7 g of EPA per day as capsules for 6 months to 14 primary hypercholesterolemic subjects. Total cholesterol, triglyceride and low density lipoprotein (**LDL**)-cholesterol levels in plasma were significantly reduced. The **LDL** cholesterol/apoB ratio and **LDL** particle size did not change. The ratio of high density lipoprotein (**HDL**)2/HDL3 cholesterol increased from 1.04 to 1.35 ($p < 0.05$), while the **HDL** cholesterol level did not change. **CETP** activity was significantly reduced. The reduction of **CETP** activity may explain the increase in the HDL2/HDL3 cholesterol ratio. These results suggest that purified EPA not only reduces **LDL** cholesterol levels but also acts on **HDL** metabolism in patients with hypercholesterolemia and therefore will be useful for the treatment of hypercholesterolemia.

L8 ANSWER 43 OF 44 MEDLINE on STN

92037798. PubMed ID: 1936105. Probucol increases **cholesteryl ester transfer protein** activity in hypercholesterolaemic patients. Franceschini G; Chiesa G; Sirtori C R. (E. Grossi Paoletti Centre, Institute of Pharmacological Sciences, University of Milan, Italy.) European journal of clinical investigation, (1991 Aug) 21 (4) 384-8. Journal code: 0245331. ISSN: 0014-2972. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Probucol, a widely used lipid lowering drug, reduces both low- and high-density (**LDL** and **HDL**) lipoprotein levels and can induce a regression of tissue lipid deposits in both animals and man. The suggested mechanism(s) involve the prevention of **LDL** oxidative modifications and, possibly, an improvement in the reverse cholesteryl ester transport system. Probucol **administration** to 10 hypercholesterolaemic patients increased the activity of the **cholesteryl ester transfer protein** (**CETP**) by 50%. The rise of **CETP** activity was significantly related with the plasma steady-state drug levels ($r = 0.51$, P less than 0.005), thus suggesting that probucol may directly stimulate CEPT synthesis and/or release. Furthermore, **CETP** activity was inversely related with **HDL**-cholesterol levels, both in the whole series of 10 patients ($r = -0.56$, P less than 0.001) and, more so, in the single individuals (r between -0.77 and -0.97), thus suggesting that the reduction of plasma **HDL**-cholesterol levels is a direct consequence of **CETP** stimulation. These findings support the

hypothesis that an improvement in the reverse cholesteryl ester transport is a major mechanism of probucol and that this may explain the drug induced plasma lipoprotein changes.

L8 ANSWER 44 OF 44 MEDLINE on STN

91307569. PubMed ID: 1854368. Diet-induced alteration in the activity of plasma lipid transfer protein in normolipidemic **human** subjects. Groener J E; van Ramshorst E M; Katan M B; Mensink R P; van Tol A. (Dept. of Biochemistry I, Erasmus University Rotterdam, The Netherlands.) Atherosclerosis, (1991 Apr) 87 (2-3) 221-6. Journal code: 0242543. ISSN: 0021-9150. Pub. country: Netherlands. Language: English.

AB Studies were performed to investigate the effect of diets rich in oleic or linoleic acids on the activity of plasma **cholesteryl ester transfer protein** (**CETP**) in normolipidemic subjects. Previous to the test diets, all subjects consumed a baseline diet rich in saturated fatty acids ("sat-diet") for 17 days. The test diets, rich in either monounsaturated fatty acids ("mono-diet") or rich in polyunsaturated fatty acids ("poly-diet"), were given for 5 weeks to 52 normolipidemic healthy volunteers. The activity of **CETP** was measured, using a method independent of endogenous plasma lipoproteins, as the rate of exchange of radioactive cholesteryl oleate between labelled **LDL** and unlabelled **HDL**. The "mono-diet" induced a statistically significant decrease in **CETP** activity (from 115 +/- 20 to 102 +/- 19 units/ml plasma, P less than 0.01), while the small decrease on the "poly-diet" (from 111 +/- 23 to 107 +/- 22 units/ml plasma) did not reach significancy. The percentual decrease in **CETP** activity induced by the "mono-diet" was higher than that induced by the "poly-diet" as was also found for the decrease in **LDL** cholesterol. In both diet groups a positive correlation was found between changes in **CETP** activity and changes in plasma total or (VLDL + **LDL**) cholesterol. The results suggest that high levels of dietary monounsaturated fatty acids may result in decreased plasma **CETP** activity, as well as **LDL** cholesterol levels. The mechanisms of these effects, and their possible interrelations, remain to be established.

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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